A Red Flag for Community-Acquired Pneumonia in the Elderly

Sir,

Advanced age is associated with defects in innate and adaptive immunity, called immunosenescence.[1] As a result, apparently immunocompetent patients become susceptible to many opportunistic infections.[2] The clinical features of sepsis are distinct in elderly individuals. We describe an elderly female patient who presented with community-acquired pneumonia, which posed a considerable diagnostic challenge, leading to significant delay in appropriate intervention.

An 84-year-old Caucasian female presented with nonproductive cough, decreased appetite, and malaise of 2 months' duration. She was initially diagnosed as right middle lobe pneumonia and had received three courses of antibiotics. However, her symptoms continued to worsen and she required 5 liters oxygen via nasal cannula. She had no history of fevers, chills, night sweats, weight loss, or skin rash. She had past history of hypertension, hyperlipidemia, and chronic atrial fibrillation.

Initial laboratory data demonstrated elevated calcium with 1,25-dihydroxyvitamin D_3, parathyroid hormone, parathyroid-related peptide, serum M-protein, and angiotensin-converting enzyme level. All primary relevant microbiology evaluations were normal. A computerized tomography (CT) scan of the chest showed partial collapse and consolidation of the right middle lobe, and a 15-mm cavitary lesion situated inferiorly [Figure 1].

The patient underwent bronchoscopy with normal airway examination, and bronchoalveolar lavage (BAL) and transbronchial biopsies (TBBx) were performed from the right middle and lower lobes, respectively. The BAL cultures were negative. The TBBx demonstrated interstitial pneumonitis with histiocytic infiltrates and vaguely formed non-necrotizing granulomas [Figure 2a and b]. The hematoxylin-andeosin (H&E) and Gomori's methenamine-silver (GMS) stains showed several yeasts morphologically consistent with *Histoplasma* species within the cytoplasm of the infiltrating histiocytes [Figure 3a and b]. The patient's serum fungal battery for histoplasma antibody and urinary histoplasma antigen were later reported as positive. Therapy with intraconazole was initiated for the diagnosis of acute diffuse histoplasmosis. Her symptoms improved remarkably, and her oxygen was weaned down. A follow-up chest X-ray at 8 weeks showed complete resolution of the lesion.

Histoplasma capsulatum is the most common endemic mycosis in the US.[3] The lungs provide a portal of entry for this fungus. Acute histoplasmosis is often self-limited, and the symptoms are usually mild in immunocompetent hosts. Ledke *et al.* noted certain age-related differences in the characteristics of histoplasmosis.[4] The asymptomatic presentation, acute histoplasmosis, chronic cavitary lesion similar to mycobacterial tuberculosis, and absence of hilar lymphadenopathy are more common in the elderly population.[4] Chronic progressive histoplasmosis, also commonly described in the elderly population, manifests with minimal symptoms but electrolyte abnormalities. Histoplasmosis characteristically causes necrotizing granulomatous inflammation,

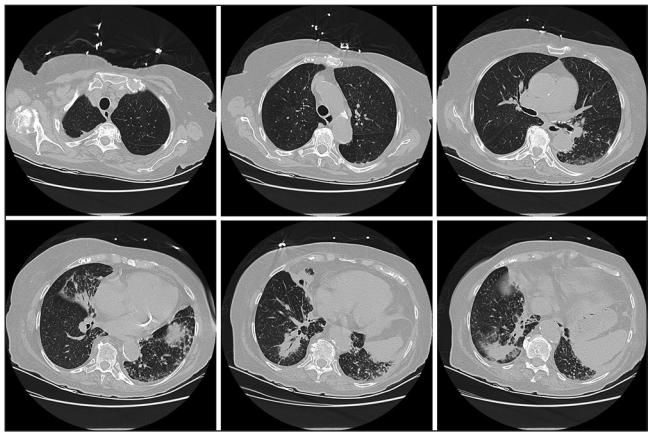

Figure 1: CT scan of chest at admission showing consolidative lesion in right middle lobe

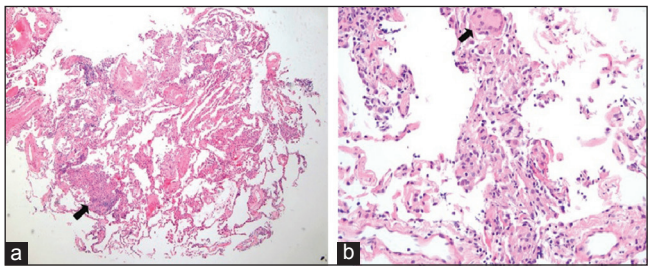

Figure 2: (a) Transbronchial biopsy showing focal interstitial pneumonitis(black arrow), H&E, 4× (b) Infiltrating histiocytes with vague non-necrotizing granuloma formation with a multinucleated giant cell (arrow)shown H&E, 10×

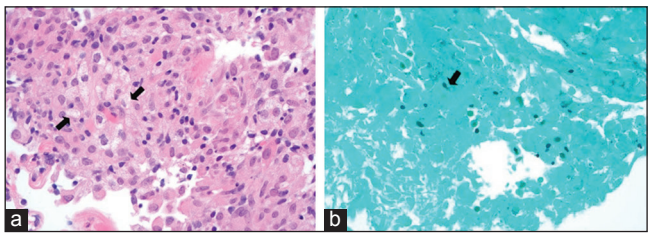

Figure 3: (a) Transbronchial biopsy showing foamy histiocytes (black arrow) in association with the interstitial pneumonitis and ill-formed non-necrotizing granulomas, H&E, 20× (b) Histoplasma yeasts within the macrophages (black arrow), GMS stain, 20×

leading to hypercalcemia, which is less likely to occur in immunocompromised individuals.

Treatment is indicated in the elderly with acute pulmonary histoplasmosis if symptoms persist for longer than a month or in case of a severe disease burden.[5] This infection is commonly treated with itraconazole in the elderly and not amphotericin, given the risk of nephrotoxicity.[4,5] Chronic progressive pulmonary histoplasmosis should be treated, even if it is minimally symptomatic.

The clinical outcome of fungal infections is also likely to be worse in elderly patients because they are less able to cope with the burden of endemic mycosis, owing to age-related changes in innate and adaptive immunity. A high index of suspicion should be harbored for acute pulmonary histoplasmosis in elderly patients presenting with atypical features of community-acquired pneumonia.

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